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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/889,203	03/13/2002	Tracey Brown	229752005700	8511

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EXAMINER	
FUBARA, BLESSING M	

ART UNIT	PAPER NUMBER
1613	

NOTIFICATION DATE	DELIVERY MODE
11/29/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

EOfficePA@mofo.com

Office Action Summary	Application No.	Applicant(s)	
	09/889,203	BROWN, TRACEY	
	Examiner	Art Unit	
	BLESSING M. FUBARA	1613	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 September 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27,30,32,33,36,38,39,42,44,45,48,50-52,57,58,61 and 63-73* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27,30,32,33,36,38,39,42,44,45,48,50-52,57,58,61 and 63-73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/16/2010 and 11/06/2009*.

4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.

5) ☐ Notice of Informal Patent Application

6) ☐ Other: _____.

DETAILED ACTION

1. examiner acknowledges receipt of request for extension of time, amendment to the claims and remarks filed 9/16/2010. The examiner also acknowledges receipt of IDS filed 9/16/2010 and 11/06/2009. Claims 27, 33, 39, 45 and 51 are amended. Claims 59, 60 and 62 are canceled. New claims 63-73 are added. Claims 27, 30, 32, 33, 36, 38, 39, 42, 44, 45, 48, 50-52, 57, 58, 61 and 63-73 are pending.

Response to Arguments

Previous rejections that are not reiterated herein are withdrawn.

Rejections in view of Amendment

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 27, 30, 32, 33, 36, 38, 39, 42, 44, 45, 48, 50-52, 57, 58, 61 and 63-73 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is new matter rejections.

4. Claims 27, 33, 39, 45 and 51 are amended to recite molecular weight range of 750,000-890,000 Da for hyaluronic acid. This molecular weight range was not envisioned at the time the application was filed.

5. Claims 27, 33, 39, 45 and 51 are amended to recite intrinsic viscosity of between 1.07 dl/gm and 112.45 dl/gm. The specification as filed does not envision intrinsic viscosity within the range recited and does not also envision that the hyaluronic acid would have an intrinsic viscosity.

6. Applicant has indicated that the specification as filed supports these amendments; that the amendment and new claims can be found in original claims, Example 2 at page 17, line 37; Example 3 at page 29, line 28; Example 12 at page 69, line 26; Example 13 at page 79, line 35, page 80, lines 4-5, page 81 and Table 4; Figures 6 and 28. But, these sections of the specification cited by applicant to provide support for the amendment and new claims do not disclose molecular weight in the range of 750,000-890,000 Da for hyaluronic acid and also do not provide support for viscosity or intrinsic viscosity in the range recited.

7. Figure 6 supports molecular weight of 890,000 Da and which was the basis for amending pages 17 and 29 of the specification on 8/17/2009 to correct attested typographical error in the disclosed molecular weight for hyaluronic acid.

8. Applicant has also indicated that intrinsic viscosity can be calculated by application of Mark-Houwink equation using the beginning and ending molecular weights in the range recited. But, the original specification made no mention of viscosity or intrinsic viscosity or viscosity of any value or intrinsic viscosity of any value. Also, the original specification made no mention of the Mark-Houwink equation that could be used to calculate intrinsic viscosities.

9. The rejection may be overcome by removing the new matter from the claims. Correction is respectfully requested.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

11. a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 27, 30, 32, 33, 36, 38, 39, 42, 44, 45, 48, 50-52 and 57, 58, 61 and 63-73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Falk et al. (US 5,985,850). The rejection is modified to account for the new claims and the amendment to the claims.

13. Falk discloses injectable formulations comprising anti-cancer agent or chemotherapeutic agent and hyaluronic acid (column 10, lines 8-59). The preferred molecular weight for the hyaluronan is less than 750,000 Daltons (claims 142, 83, 84 and 92). The anti-cancer drug or chemotherapeutic agent of Falk, specifically, methotrexate and 5-fluorouracil (claims 38 and 79) meet the chemotherapeutic agents of claims 27, 32, 33, 38, 39, 44, 45, 50 and 51. The method of enhancing the efficacy of the chemotherapeutic agent in claims 27 and 33, the method of overcoming acquired resistance of cancer cells to chemotherapeutic agents in claim 39 comprises intravenous administration of effective amount of hyaluronan and chemotherapeutic agent to a subject in need thereof. Falk's method of administration of the hyaluronan containing composition is by intravenous, intra arterially, intraperitoneally, intrapleurally, transdermally, topically, rectally, or by direct injection of the of the composition into a tumor (column 10, lines 48-55), which meets the mode of administration of the claims such that the effect of the composition after administration, that is, enhancing the efficacy of the chemotherapeutic agent in

claims 27 and 33, the method of overcoming acquired resistance of cancer cells to chemotherapeutic agents in claim 39 are met. The intrinsic viscosity recited in claims 27, 33, 39, 45 and 51 and the polydispersity of the hyaluronan recited in claims 57, 58, 61 and 67 are the properties of the hyaluronan so that the hyaluronan of Falk having these intrinsic properties meets the requirements of claims 27, 33, 39, 45 and 51 and 57, 58, 61 and 67.

14. Falk does not use hyaluronic acid having molecular weight range between 750,000 Da and 890,000 as recited in generic claims 27, 33, 39, 45 and 51. However, while Falk uses hyaluronic acid having molecular weight of less than 750,000 Da but greater than 150,000 Da in specific dosage forms (see claims 42, 83, 84 and 92) Falk contemplates the use of HA having higher molecular weight and the requirement is that the composition be diluted to permit administration that does not coagulate (column 19, lines 32-34) and specifically HA having molecular weight in the range of 750,000 to 1,200,000 is suggested (column 18, lines 64, 65) with the range of 750,000 to 1,200,000 encompassing the recited range. Therefore, taking the general teaching suggestion of Falk, the person of ordinary skill in the art at the time the invention was made would have reasonable expectation of success that using hyaluronic acid having molecular weights in a range of 750,000 to 1,200,000 and using the appropriate dilution to provide a composition having a viscosity such that the composition does not coagulate, would be suitable carrier vehicle having desired viscosity that would provide the anticipated therapeutic composition for successful systemic delivery of cytotoxic agents so that claims 27, 33, 39, 45 and 51 are rendered obvious.

15. A molecular weight of 890,000 Da lies within the suggested range of 750,000 to 1,200,000 Da so that the molecular weight of 890,000 Da in claims 30, 36, 42, 48, 52, 63, 65, 68, 69 and 70 would be obvious; a molecular weight of 750,000 lies within the suggested range of

750,000 to 1,200,000 Da so that the molecular weight of 750,000 Da in claims 64, 66 and 71-73 would also be obvious.

16.

Response to Arguments

17. Applicant's arguments filed 9/16/2010 have been fully considered but they are not persuasive.

18. Applicant argues on pages 17-20 of the remarks that Falk does not teach intravenous administration of HA having molecular weight of between 750,000 and 890,000 and that HA having higher molecular weight is administered after intravitreal and other intraocular surgery; that HA of higher molecular weight has been known to be used intraarticularly and for topical applications as barrier to water and microorganisms.

19. Response: The rejection is not an anticipatory rejection. Falk teaches the anticancer agents of the claims; Falk teaches HA in combination with the anticancer agent and suggests that HA having molecular weight within the range of 750,000 to 1,200,000 Da can be used with a further suggestion to dilute such a composition to avoid coagulation. The second paragraph (column 19, lines 40-43) after the suggestion to use HA having molecular weight, Falk talks about obtaining unexpected results from the combination of HA and therapeutic agents. Therefore, taking the teaching of Falk, the skilled artisan would be led to using HA having molecular weight within the range of 750,000 to 1,200,000 Da. Applicant obtains enhanced efficacy of chemotherapeutic agent by systemically administering composition that contains HA and therapeutic agent. In the same way, the systemic administration of composition comprising HA and therapeutic agent as contemplated by Falk would also enhance the efficacy of the chemotherapeutic agent. Therefore, when the teaching of Falk is considered as a whole, the

artisan would have good reason to pursue the known options of intravenous administration of HA having molecular weight within the disclosed range with the added disclosure by Falk to dilute the composition so as to reduce the coagulation.

20. "Obviousness does not require absolute predictability of success."

21. The declaration filed 9/11/06 and 8/19/08 by Dr. Tracey Brown have been addressed in the office actions dated 10/30/2008 and 3/25/2010. It was noted on 3/25/2010 that on the whole, because the claims have not recited amounts of the HA and the chemotherapeutic agent, the declaration using specific concentration of chemotherapeutic agents is not commensurate with the claims.

22. No claim is allowed.

23. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

24. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

25. **Request for Interview**: The applicant had requested the examiner to call the applicant to address any remaining issues that can be taken care in order to move the application towards

allowance. However, the issues remaining are many and the office action attempts to address those issues.

26. Applicant is however invited to call the examiner to set up interview to discuss the issues and to explore ways of moving the claims closer to allowance.

27. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BLESSING M. FUBARA whose telephone number is (571)272-0594. The examiner can normally be reached on Monday to Thursday from 7 a.m. to 5:30 p.m.

28. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brian Y. Kwon can be reached on (571) 272-0581. The fax phone number for the organization where this application or proceeding is assigned is 7571-273-8300.

29. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Blessing M. Fubara/
Primary Examiner, Art Unit 1613